CLAIMS

1. An isolated and purified nucleic acid encoding a GRK4 protein having an R65L, A142V mutation, an R65L, A486V double mutation, or an R65L, A142V, A486V triple mutation.

2. An oligonucleotide which specifically hybridizes to a *GRK4* gene having a sequence that encodes an R65L mutation, an A142V mutation, an A486V mutation, an R65L, A142V double mutation, an R65L, A486 double mutation or an R65L, A142V, A486V triple mutation.

3. An oligonucleotide primer which hybridizes to exon 3, 5, 8, 14 or 16 of a *GRK4* gene, and is useful in amplifying a DNA sequence including nucleotides 431 to 503 (exon 3), 594 to 697 (exon 5), 857-995 (exon 8), 1662 to 1798 (exon 14), and 1937 to 1991 (exon 16) of said gene.

4. A method of identifying individuals predisposed to essential hypertension, comprising:

obtaining kidney cells having a D1 receptor and expressing *GRK4* from said individual; and

assaying said cells to determine extent of post-translational modification of said D1 receptor, wherein a change in post-translational modification of said D1 receptor relative to extent of post-translational modification of a D1 receptor in kidney cells having a D1 receptor and expressing *GRK4* isolated from a normotensive individual, is indicative of a predisposition to essential hypertension.

5. The method of claim 4, wherein said cells are assayed for the extent of palmitoylation of said D1 receptor.

6. The method of claim 4, wherein said cells are assayed for the extent of phosphorylation of said D1 receptor.

7. The method of claim 4, wherein said cells are assayed for hyperphosphorylation of said D1 receptor.

8. The method of claim 4, wherein said kidney cells are renal proximal tubule cells or cortical duct collecting cells.

9. A reconstituted system that measures GRK activity, comprising GRK4 and a GRK4 substrate.

10. The reconstituted system of claim 9, wherein said GRK4 substrate is a D1 receptor or a functional fragment thereof.

11. The reconstituted system of claim 10 which is a whole cell that expresses said GRK4 and said GRK4 substrate.

12. The reconstituted system of claim 11, wherein said whole cell is a Chinese hamster ovary cell transfected with a first heterologous gene encoding a D1 receptor and a second heterologous gene encoding a GRK4 protein associated with hypertension.

13. The reconstituted system of claim 9, wherein said GRK4 protein is associated with essential hypertension.

14. A complex between a GRK4 protein associated with hypertension and an agent which provides a detectable conformational change in said GRK4 protein upon interaction with a substance being analyzed for anti-hypertensive activity.

15. An immortalized human proximal tubular cell.

16. An isolated and purified renal proximal tubular cell obtained from a hypertensive human.

17. The isolated and purified renal proximal tubular cell of claim 16, which is immortalized.

18. A transgenic animal, comprising a diploid genome comprising a transgene encoding a GRK4 protein which is expressed in renal cells to produce said GRK4 protein, and wherein expression of said transgene causes said transgenic animal to exhibit a state of essential hypertension compared to a normotensive animal whose renal cells do not express said GRK4 protein.

19. The transgenic animal of claim 18, wherein said renal cells have a decreased ability to reject sodium compared to a normotensive animal whose renal cells do not express said GRK4 protein.

20. The transgenic animal of claim 18, which is a rodent.

21. The transgenic animal of claim 18, which is a mouse.

22. A method of identifying putative anti-hypertensive agents, comprising:

adding at least one candidate agent to the reconstituted system of claim 9; and

detecting GRK4 activity, wherein a change in said activity is indicative of a putative anti-hypertensive substance.

23. The method of claim 22, wherein said step of detecting GRK4 activity comprises measuring adenylyl cyclase activity.

24. The method of claim 22, wherein said step of detecting GRK4 activity comprises adding a substrate to which phosphate can be added, and a phosphate source to said culture, and measuring phosphorylation of said substrate.

25. A method of identifying putative anti-hypertensive agents, comprising:

contacting at least one candidate agent with the complex of claim 14, and detecting whether a conformational change in said GRK4 occurs, wherein a conformational change is indicative of putative anti-hypertensive activity.

26. The method of claim 25, wherein said detecting is conducted by spectrophotometry, fluorescence, nuclear magnetic resonance, evanescent wave technology or atomic force microscopy.

27. A method of identifying putative anti-hypertensive agents, comprising:

adding at least one candidate agent to a culture of immortalized kidney cells that express a D1 receptor and GRK4 isolated from a hypertensive animal; and

detecting a change in transduction of a dopaminergic signal in said cells, wherein a change in transduction of a dopaminergic signal is indicative of putative anti-hypertensive activity.

28. A method of identifying putative anti-hypertensive agents, comprising:

comparing electrolyte output of a first transgenic animal of claim 18 administered said agent, and a second transgenic animal of claim 18 not administered said agent, whereby a putative anti-hypertensive agent is identified by increased electrolyte output of said first transgenic animal as compared to said second transgenic animal.

29. A method of increasing natriuresis, comprising administering to an essential hypertensive individual a drug that interacts with GRK4 so as to increase natriuresis in said individual.

30. The method of claim 29, wherein said drug changes expression of *GRK4* in kidney cells of said hypertensive individual.

31. The method of claim 29, wherein said drug comprises antisense RNA that binds *GRK4* mRNA or DNA.

32. The method of claim 29, wherein said drug comprises a ribozyme that cleaves *GRK4* mRNA or pre-mRNA.

33. The method of claim 29, wherein said drug comprises a dominant negative mutant DNA molecule.

34. The method of claim 29, wherein said drug binds GRK4 protein.

35. An oligonucleotide which specifically hybridizes to *GRK4* mRNA *in vitro* or *in vivo*.

36. The oligonucleotide of claim 35, which is an antisense RNA molecule.

37. The oligonucleotide of claim 35, which is a dominant negative mutant DNA molecule.

38. A ribozyme that cleaves *GRK4* mRNA or pre-mRNA.